

REMARKS

Request for Reconsideration

Applicants have carefully considered the matters raised by the Examiner in the outstanding Office Action but remain of the opinion that patentable subject matter is present.

Applicants respectfully request reconsideration of the Examiner's position based on the amendments made to the claims, the attached Declaration of Mr. Nakajima and the following remarks.

Claims Status

Claims 21-46 are pending in this Application.

Claims 43-45 have been amended herein to correct obvious typographical errors. It is clear that Claim 42 provides the antecedent basis for the additive which is recited in dependent Claims 43-45. Claim 46 recites the addition of ethanol. Support for this claim can be found on page 24, lines 5-19, as well as Example 1 on page 44. Respectfully, no new matter has been added by way of these amendments.

Double Patenting Rejection

Claims 21, 22 and 26 had been provisionally rejected on the grounds of non statutory obviousness-type double patenting based on Claims 1, 4, 6, 8-10 and 19 of copending Application 11/180,849; and Claims 21, 22, 25, and 27 had been provisionally rejected on the grounds of non statutory obviousness-type double patenting based on Claims 1, 5-8, 10-11 and 14-17 of copending Application 11/187,397.

Applicants hereby request that these rejections be held in abeyance until such time as an indication of patentable subject matter. At that time, the claims can be evaluated to determine if the double patenting rejection is still valid and whether a timely Terminal Disclaimers need be filed.

Prior Art Rejection

Claims 21-43 had been rejected as being unpatentable over a combination of Otake or Castor in view of Sachse and Mackaness. Claims 21-42, 44 and 45 had been rejected as being unpatentable over a combination of Otake or Castor in view of Sachse and Klaveness.

The Examiner has used Otake or Castor to teach formation of liposomes using supercritical carbon dioxide. The Examiner had recognized that neither Otake nor Castor teach forming the liposome with an iodine compound or the inclusion of a water soluble amine compound in the preparation of a liposome. For the inclusion of the iodine or water soluble amine compound in the liposome, the Examiner had turned to the secondary references of Mackaness or Klaveness. In order to address the surprising and unexpected results which are obtained in the present Invention, comparative tests have been made and those tests are reported herein by way of a Declaration of Mr. Nakajima.

Mr. Nakajima's test results clearly demonstrate that the preparation of a liposome including a water soluble non-ionic iodine compound by way of supercritical carbon dioxide shows surprising and unexpected results in the weight percent of the iodine compound that is included in the vesicle based on the total weight of the iodine compound. Specifically, Mr. Nakajima ran Example 1 of Mackaness and tested it to determine that the weight percent of iodine compound was 0.5, Sample A. Mr. Nakajima then went on to take Example 1 of Otake and run Example 1 of Otake using the contrast medium in Mackaness. For the liposome formed by this process, Mr. Nakajima found that the

inclusion rate was 17%, Sample D. As the Examiner will appreciate, an increase by a factor of 34 in the inclusion is surprising and unexpected in light of Samples B and C, where a pharmacological compound using both Mackaness and Otake was prepared and the increased proportion of inclusion was only 2.5. Such superior results cannot be predicated from the mere reading of the Prior Art.

In other words, Sample B is the process of Mackaness wherein a pharmacological compound has been used in place of the iodine compound and Sample C is the process of Otake using a pharmacological compound. Sample B had a proportion of inclusion of 6 and Sample C had a proportion inclusion of 15. Thus, one of skill in the art would expect an increase in the amount of the inclusion compound to be only on the order of 2.5. Continuing the logic, one of skill in the art would expect the inclusion of iodine in Otake to be only 1.25, not 17. An increase of 34% versus an increase of 2.5% is truly surprising and unexpected based on the teachings of the Prior Art.

Mr. Nakajima went one step further. Mr. Nakajima included ethanol when forming the liposome with the iodine compound and found that the inclusion ratio was 20%. As the Examiner will appreciate, a 40-fold increase in the inclusion ratio is also

surprising and unexpected based on the teachings of the Prior Art.

Respectfully, based on the Declaration evidence, as presented herein, Applicants have demonstrated that their Invention provides surprising and unexpected results compared to the teachings of the Prior Art.

In view of the foregoing, it is respectfully submitted that the Claims, as presented herein, are patentable over the references taken alone or in combination.

Conclusion

In view of the foregoing and the enclosed, it is submitted that the Application is in condition for allowance and such action is respectfully requested.

Should any fees or extensions of time be necessary in order to maintain this Application in pending condition, appropriate requests are hereby made and authorization is given to Account #02-2275.

Respectfully submitted,

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Attached: Executed Declaration of Mr. Nakajima signed
on March 12, 2008.